RESEARCH PROTECTIONS UPDATE

News and Comments on the Protection of Human Subjects in Navy and Marine Corps Research

Volume 11, Number 1 ***March 2021***

DIRECTOR'S CORNER

This issue highlights the topic of innovation and includes articles from several commands who were willing to share their innovative approaches to conducting human subjects research during the COVID-19 pandemic. Innovation is not just a buzzword; it is a state of mind. Innovation looks at a challenge and says "what if?" and "why not?" Innovation is a process and an outcome and it is the key to staying ahead of our adversaries.

Innovation is also at the heart of human subjects research and human subjects research protection. As Professor Chris MacDonald, ethics educator, speaker and author of "The Business Ethics Blog" notes, innovation is an ethical issue as risks and benefits are weighed in the pursuit of the new or unknown. Within Navy Human subjects research, one sees the results of positively pushing boundaries- solving problems and forging new possibilities, while maintaining dignity and respect of participants. From the exploration of ideal sleep cycles in extreme environments to the effectiveness of non-lethal weapons, innovation is necessary to ethically increase warfighter readiness. In response to COVID-19, DON HRPP updated the process for conducting site inspections and assist visits through the adaptation of Microsoft Teams. DON HRPP continues to seek ways to apply innovation to existing processes, along with new processes and possibilities in the coming year. Of course, to harness the benefits of innovation, we must embrace diversity. As we recognize in this issue Martin Luther King, Jr. Birthday (January 18), Black History Month (February 1-28), and Women's History Month (March 1-31) we must keep in mind that inclusion of diverse experiences, perspectives, and talents is the foundation for innovation to thrive. People, as discussed by the Surgeon General in the previous edition of the RPU, is listed first for a reason. It is with and for the people supporting human subjects research in innovative fashion that we begin this edition.

-CDR Leedjia Svec

Innovation in the Military

By Chidima Ioanou

Innovative ideas, whether as a response to an urgent problem or a natural evolution of some technology, have a foundation set in creating solutions that would be advantageous to its user. Innovation through research and development (R&D) has long since been part of the U.S military history. In the late 1800s, during the Spanish-American war, the devastating effects of yellow fever were felt in battle. It was reported that more military casualties were as a result of yellow fever than combat.[1] Following the establishment of the Yellow Fever Commission, in 1900, Major Walter Reed led breakthrough research establishing that the transmission of yellow fever was through mosquitos.[2] During World War II, the advantages of being able to apply remote sensing technology to detect enemy aircrafts were clear. Research at the Naval Research Laboratory (NRL) led to the development of the first U.S radar, the XAF. These radar units were installed on several ships which aided the U.S Navy in victories during World War II.[3]

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Also in this Issue:

Innovation in the Military *(continued from page 1)*

The process of innovation generally follows the path of identifying a problem or a gap, generating an idea to solve the problem, and testing and development of the idea/solution. Innovation in the military often bears its roots in experiences on battle fields, in military hospitals, and in research labs. In the Navy, inventive ideas are developed to increase survivability, increase warfighter performance, and to enhance readiness. The Department of the Navy is steadfast in its commitment to innovation as it assists in achieving Naval superiority and medical readiness. The Navy establishes research collaborations between Components, industry and academic partners. These collaborations foster an environment that expands technological and scientific expertise which ultimately leads to enhanced research and development for our warfighters. In fact, some products of Navy R&D such as the global positioning system (GPS)[4] have had lasting impact on the civilian world as GPS is routinely used in our current daily lives. As we reflect on the importance of military innovation, this article highlights a couple of (early and current) examples of innovation in Navy history;

"In the Navy, inventive ideas are developed to increase survivability, increase warfighter performance, and to enhance readiness."

The Wire Basket Stretcher invented by Rear Admiral Charles Stokes[5]

During the Spanish-American War a Navy physician by the name of Charles Stokes observed the difficulties is transferring the wounded. At the time the commonly used modes of ambulating the injured included transfer boards. Stokes, developed the wire basket stretcher (also known as the Stokes stretcher) which combined the capabilities of a stretcher and a splint into one. By, January 1906, the wire basket stretcher was adopted by both the Navy and the Army.

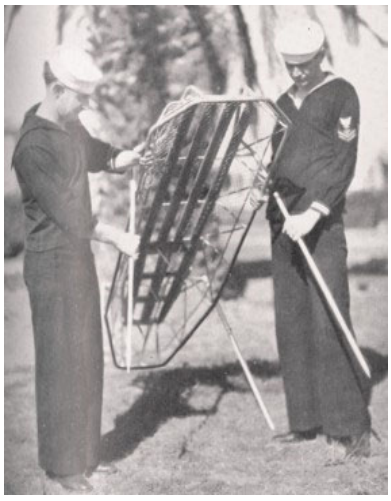

Photo credit. BUMED archives

Bacteriophage-Phage Therapy on Acinetobacter baumannii Infection at Naval Medical Research Center (NMRC)[6]

As drug resistant bacteria becomes a growing concern,[7] in 2016 researchers at NMRC announced that they successfully treated Acinetobacter baumannii, a drug-resistant infection with phage therapy. Phage therapy is the process of using bacterial viruses to treat bacterial infections.[8] Acinetobacter is a commonly found in the environment. It can easily spread from contaminated surfaces such as equipment if not properly cleaned. Acinetobacter can cause infections in wounds, blood and the urinary tract and unfortunately this group of bacteria are resistant to many antibiotics.[9] The further development of phage therapy has obvious beneficial implications to military health.

References

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3) https://www.history.navy.mil/browse-by-topic/exploration-and-innovation/radar-sonar.html

4) https://www.nasa.gov/directorates/heo/scan/communications/policy/GPS_History.html

5) Sobocinski, Andre. "A Medical Device for the Ages: Historical Notes on Admiral Stokes Stretcher." Retrieved from https://navymedicine.navylive.dodlive.mil/archives/9189

6) https://www.medicineandthemilitary.com/officer-and-medical-training/military-medical-advancements

7) https://www.cdc.gov/drugresistance/biggest-threats.html

8) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5547374/

9) https://www.cdc.gov/hai/organisms/acinetobacter.html

Conducting Human Subject Research (HSR) During the COVID-19 Pandemic: Command Innovative Approaches

Conducting hsr during the COVID-19 global pandemic has been an unprecedented challenge. Creating and implementing processes that ensure subject safety, data integrity and key personnel well being, all while still meeting Federal, State, Component and Command-specific requirements is a daunting task. In the article below, Commands share their innovative approaches in navigating and accomplishing this very important duty.

Naval Air Warfare Center Aircraft Division (NAWCAD)

Initial steps here at the NAWCAD last March was to temporarily pause all NAWCAD sponsored and conducted research until we had a better understanding of COVID and it impacts on safely conducting HSR.

Our second step was to survey our Principle Investigators and work center managers to understand what supplies they had on hand and what additional supplies they needed to safely implement cleaning procedures of laboratory spaces and equipment, and if adequate PPE was available for use. This process took approximately 6 weeks until we were satisfied our HSR could safely resume.

Third, we required all current HSR protocols to be modified to include the additional risks and mitigations of possible pathogen exposure while participating in HSR. We also requested any investigator, test team member or test subject that tested positive during the testing period be reported to the IRB so we could ensure it was included in the command tracking reports.

The NAWCAD has implemented a mandatory temperature check for all personnel entering our buildings. Some investigators have taken the extra step of purchasing non-contact thermometers and checking subject temperatures before each data trial.

I think DON HRPP and Kristin Jones (our DON HRPP POC) were very quick to give the NAWCAD guidance on how to proceed in the pandemic environment. We were able to quickly pause, get a grasp of the situation and safely resume HSR with minimal interruption. To date, the NAWCAD has not had any reported incidents of COVID 19 being contracted or spread during any of our HSR studies.

Naval Submarine Medical Research Laboratory (NSMRL)

On March 11, 2020, the World Health Organization (WHO) declared the novel coronavirus outbreak a pandemic. Two days later, U.S. President Donald Trump declared a national emergency and restricted travel from European countries into the U.S. In the coming days and months, schools would close their doors, restaurants, bars, gyms, stores, and entertainment venues would shutter, and governors across the country would issue stay-at-home orders, quarantine protocols, and mask mandates. In those early days, fear and uncertainty were rampant while scientific and evidence-based knowledge about the spread, severity, and control of the virus were sparse. Within days of the WHO announcement, and in line with local and higher level Department of Defense and Department of Navy directives, NSMRL implemented an initial fourteen day lab closure and a two-week hold on all in-person interactions for research. At the time, no one envisioned the pandemic would persist a year later.

One exception to the hold on human subject research was studies that were secondary to military operations – the reasoning was that the research added no more interaction than the operation itself, and thus would not pose a greater health risk to the operation. Given this exception, one study that was in progress on a deployed submarine was allowed to proceed as planned because the research team was already embedded underway with the crew.

Early into the two-week hold on human subject research, it became clear that COVID-19 restrictions would be prolonged and the path for continued research would need to be repaved as we moved into an uncertain future. Much of NSMRL's research projects involve human subject research, and a prolonged hiatus from such research would jeopardize the command's ability to complete its mission. Therefore, it quickly became apparent that we would need to be agile, adaptive, and creative in finding solutions to continue critical human subject research while also adhering to safety guidelines that would protect the health of study participants, researchers, and ultimately, the nation.

At the end of March 2020, NSMRL convened an

Conducting Human Subject Research During the COVID-19 Pandemic:

Command Innovative Approaches *(continued from page 3)*

Naval Submarine Medical Research Laboratory (NSMRL)

emergency IRB meeting to discuss the current restrictions and plan a way forward. Among the topics of discussion were:

- An informal review of major New England university websites showing that all human subjects research was on hold indefinitely unless the research directly benefitted the subject (i.e. studying a coronavirus treatment on a subject effected by the disease),
- Depending on the length of COVID-19 restrictions, there could be an issue meeting both grant expenditure milestones by the end of the fiscal year and research execution goals. While sponsors understood the circumstances, there was concern among principal investigators that too long of a delay could jeopardize lines of research.
- There was general consensus that, in the near term, bringing subjects into the lab was too risky. However, if restrictions continued for several months and means of mitigation became clearer, research could potentially be restarted safely.

Based on the recommendations of the IRB committee following this meeting, NSMRL's Commanding Officer, CAPT Kim Lefebvre, MSC, USN, declared that NSMRL would institute a default prohibition of human subject interaction for all protocols. However, this would not be an absolute decision. Rather, each protocol would be decided on a case-by-case basis by request. The command drafted an instruction for a phased reopening plan that aligned with the parent base guidelines. This instruction included a form to request resumption of research. Considerations for resumption included military need, required a COVID-19 mitigation standard operating procedure, and balanced the need to conduct human subject research with appropriate risk reduction and safety concerns. NSMRL's Commanding Officer had final approval on all such requests.

Under this new procedure, and with rapid restructuring of planned data collection efforts, several studies that had been paused were able to restart. For example, an ongoing survey-based study was converted to an online format that allowed participant responses without any in-person interaction. In addition, new studies were approved. For these new studies and those that were approved to resume, NSMRL acquired effective Personal Protective Equipment (PPE) for participants and study managers, and all studies adhered to CDC distancing and protection guidelines.

After nearly one year of COVID-19, NSMRL has found an approach that aims to balance risk with the need to continue important research for the DoD. At the time of writing, all measures remain in place. We continue to incorporate emerging new guidance into all human subject research. The IRB still meets on a regular basis to review proposed protocols. Though there are new considerations that were not present a year ago, we are confident that we have adapted successfully to this "new normal" and have a safe way to move forward with our mission, our research, and our commitment to protecting our people.

Naval Medical Research Unit Dayton (NAMRU-D)

Our Command's initial response to the pandemic was to screen any scheduled participants about flu like symptoms and their proximity to others with illnesses in the past two weeks. At the time, we only had three studies with scheduled data collection sessions. However, shortly afterwards Ohio declared a health emergency with a stay at home mandate and our Commander put a halt to all human subjects research. We did not have on-going treatment studies so we were able to stop data collection visits immediately.

During the several months we stopped research, the IRB leadership and NAMRU-D physician worked to develop a screening process for all active protocols to follow. We required the study teams to follow the current COVID-19 mitigation practices recommended by the CDC, state of Ohio, Wright Patterson Air Force Base, and ultimately NAMRU-D. Since recommendations changed daily or weekly we wanted to remain flexible rather than commit to a specific SOP. We also developed a more specific form for PIs to make a request to resume their research. The form asked what procedures they would implement to safely resume data collection. An amendment was not required for mitigation measures like COVID-19 screening questions, wearing masks, and increasing cleaning procedures. This was part of our Command's overall COVID-19 policy and forms were reviewed and approved by the IRB Chair/ Vice Chair before any new data collection could occur.

I believe our best strategy during the pandemic was reaching out to other IRBs for their ideas and guidance. We all struggle with making the right decision to protect our participants from additional risks and harms and talking through the problem with people outside your institution can give you valuable insights into the kinds of processes that could work best.

Conducting Human Subject Research During the COVID-19 Pandemic:

Command Innovative Approaches *(continued from page 4)*

Naval Medical Research Unit 6 (NAMRU-6), Peru

In Peru, a national lock down was mandated by the Peruvian government in response to the COVID-19 pandemic. This first lock down started on 16 March 2020 and almost all economic, educational and social activities were stopped. Only basic activities remained active and open. A few days earlier, NAMRU-6 Research Administration Program (RAP) had completed the training and authorization process for tele-working, in anticipation of a potential lock down. Below were RAP's initial steps:

- Ensured authorization to tele-work was received from the NAMRU-6 leadership.
- Identified the equipment needed to take to our houses, completed the loan paperwork and enlisted the help of colleagues who were willing to help.
- Identified the impact of protocol suspension on participants' welfare. Luckily, because of our current research portfolio, no therapeutic clinical trials were in process, so there was no negative impact. NAMRU-6, at the time, had a portfolio of 01 clinical trial, 16 observational studies enrolling subjects, and 16 observational studies closed to enrollment.
- Emailed all Principal Investigators (PIs) and provided them with guidelines on how to submit Planned Protocol Deviations to the IRB via RAP.
- Between March and April 2020, PIs from 16 observational studies that were actively enrolling submitted their Planned Protocol Deviations to RAP informing which protocol activities were going to be temporarily stopped. Submission of these deviations to the protocol took 20 days approximately because several Investigators did not have early access to their research files or their work computers and travel to work was not allowed.
- Identified with the help of information technology (IT) personnel, a secure electronic platform to conduct IRB and or RAP/Investigator meetings.
- Drafted a standardized SOP on how to conduct virtual IRB meetings. It was submitted for review and gained approval from the IRB Chair and Research Science Director (RSD). It was then sent to DON HRPP for feedback. NAMRU-6 IRB members and investigators were provided a copy once the SOP was implemented.

By October 2020, the lockdown became more flexible and different economic activities were resumed**.** RAP was informed that 04 protocols were preparing to submit the documentation to the IRB to re-start enrollment activities and to obtain the corresponding local health authority by official letter since numbers of COVID-19 cases were getting lower in some regions of the country. Below are NAMRU-6's steps to restart human subject research (HSR):

- PIs developed a safety protocol and training for their study teams in the field to raise awareness and self-care against the virus. Personal protective equipment (PPE) was also shipped to study sites planning to re-start activities. RAP ensured all protocols were using a similar safety protocol which could be adapted to each protocol circumstance.
- Verbal consent was strongly recommended, given the fact that all but one of NAMRU-6 protocols were minimal risk.
- A discussion is currently in place with the information technology (IT) team in order to identify a safe, DOD-approved platform for e-consent.

By January 2021, only 01 protocol was active. The other approved protocols were still implementing their protocol specific logistics to restart. An important issue for RAP was to assess how the start of the studies would impact the NAMRU-6 limited footprint in Lima, particularly because of the second wave of COVID-19. Discussions were held with each PI to assess their needs for sample testing to include testing for COVID-19 in Lima, as part of their restarting process.

In reflecting on NAMRU-6's response to research during the COVID-19 pandemic, here are some final thoughts:

- Supervisor's (CO, XO, Research Science Director) attitude towards the well-being of the staff proved to be essential for RAP and Investigators. It allowed everyone to focus on mitigating the spread of COVID-19, in spite of the overall concern of not being at work, and getting the job done. Personnel safety was a top priority.
- Amazing IT support is essential to teach, guide, and rescue the staff as they waded through new platforms and communication systems.
- Commitment of RAP staff, not only in our efforts to implement the first tele-working program a week after the lockdown, but also in responding to communication at odd hours and keeping our high standards in serving the Science Directorate at the Command.

Conducting Human Subject Research During the COVID-19 Pandemic:

Command Innovative Approaches *(continued from page 5)*

Naval Medical Research Unit 6 (NAMRU-6)– Peru

- Commitment of the PIs to comply with the guidelines and regulations during this situation and during restrictions that were always changing (reopening Phase 0 to Phase 1 to Phase 2 and back to Phase 1).
- Timely communication became more important than ever to be able to execute HSR during the pandemic. Also, conducting HSR during these complex times involve a great deal of flexibility to identify new processes, such as the informed consent processes, and in-depth knowledge of the situation facing the local health posts and communities with cases and deaths by COVID-19. Overwhelmed health care centers and overburdened health personnel are not conducive to detailed research processes.
- Careful decision making during a fast changing situation requires balancing between what is realistic and what is not safe, thus realistic expectations for conducting HSR that ensures subjects' safe participation need to be discussed with Sponsors. Open and honest conversations are required as well as understanding that all partners involved agree to be responsible.
- Never compromise on subject safety or data quality; it is better to say no to a study/Sponsor than guess on safety and quality, even if the study objectives are scientifically important and within the command's mission.
- Finally, emotional well-being is also important. NAMRU-6 employees set up a message group that allowed us, not only to gather in support of our colleagues who were ill but to pass critical information on how members of our command could help our fallen colleagues and their families. Having this group for emotional support, we were not isolated and we knew we had a larger force to care for each other.

"Never compromise on subject safety or data quality; it is better to say no to a study/Sponsor than guess on safety and quality, even if the study objectives are scientifically important and within the command's mission."

The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government.

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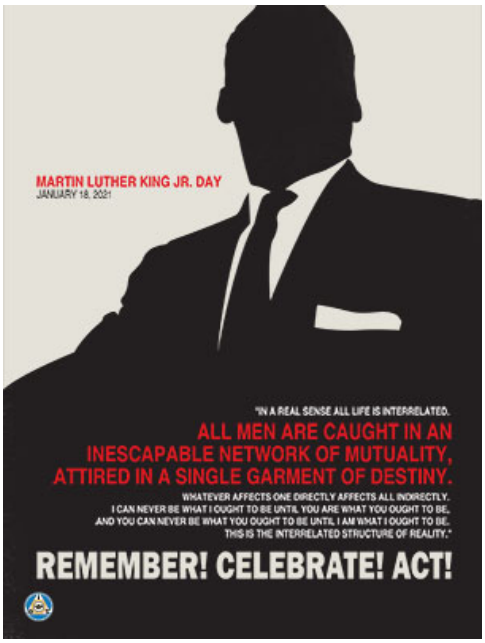
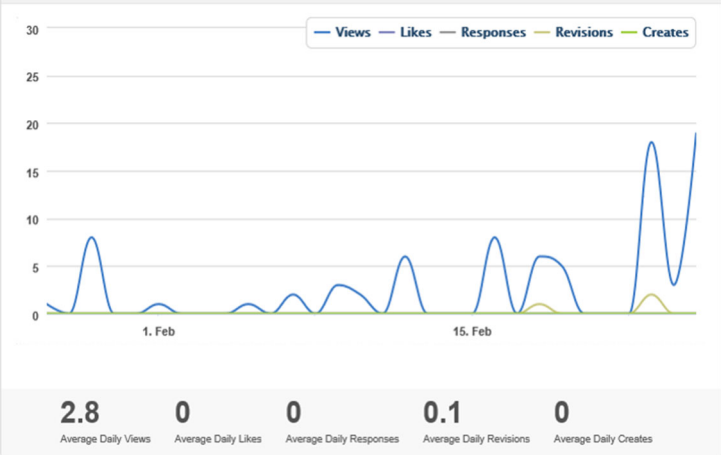
Special observances such as Martin Luther King, Jr. Birthday (January 18), Black History Month (February 1-28), and Women's History Month (March 1-31), are conducted to celebrate achievements, recognize struggles and to promote understanding.

"The ultimate measure of a man is not where he stands in moments of comfort and convenience, but where he stands in times of challenge and controversy."
- Dr. Martin Luther King Jr.



For more ways to celebrate diversity, please see observance materials provided by the Defense Equal Opportunity Management Institute at
https://www.defenseculture.mil/

DON HRPP Quality Assurance Activities



DON HRPP quality assurance activities include data collection associated with DON HRPP communications. This quarter, emails from DON HRPP that reference the DON HRPP milSuite page correspond with a subsequent increase in views of the DON HRPP milSuite group page. A DON HRPP email was sent to a group of contacts on 22 February 2021. The email referenced the DON HRPP milSuite group. Following, there was a spike in views of the DON HRPP milSuite group for the next several days.

DON HRPP will continue to collect and assess data to examine processes and methods to improve communication between DON HRPP and DON Commands.

WELCOME!!

DON HRPP welcomes new Human Research Compliance Analyst, Ms. Thomasena Williams. Ms. Williams joined DON HRPP in March 2021. She has 7 years of experience in human research protections, and IRB administration and management. Prior to joining DON HRPP, she served as the IRB Manager at Prisma Health in Columbia, South Carolina. Ms. Williams comes to DON HRPP with experience that includes research education, compliance, and accreditation. She is a graduate of Medical College of Georgia where she obtained a Bachelor's of Science degree in Health Information Administration. She also holds a Masters of Public Health from Walden University.

Ms. Williams shares that she became interested in community and public health in 1989 while working for the Bureau of Laboratories in Washington, D.C. as a microbiology lab technician in infectious diseases. She relocated from her birthplace of Washington, D.C. to Augusta, Georgia in 2000. She lived in Augusta, Georgia for 15 years and worked at the Medical College of Georgia in the following roles; histology technician, blood bank technician, tumor bank coordinator, and research laboratory manager at the college's Institute of Molecular Medicine and Genetics. She has also served as a Health Sciences and Public Health College Educator at Grand Canyon University and as Associate Academic Dean for Virginia College.

Ms. Williams has three daughters, and two grandchildren. Outside of work she enjoys community service activities involving her church and charitable organizations, family time, cooking, crochet projects, and lots of laughing.

DON HRPP News!!

- In February 2021, DON HRPP successfully conducted its' first ever Virtual Site Inspections. The virtual visits were conducted via the Microsoft Teams platform.
- Contact information for Department of the Navy (DON) Human Research Protection Officials (HRPOs) was posted on DON HRPP's milSuite site. The purpose of this posting is to encourage collaboration among Navy HRPOs. This list can be accessed on the DON HRPP milSuite site via the following link: https://www.milsuite.mil/book/docs/DOC-949611

We Need Your Help!

Get a BZ from RPU

Have a "Good News" story or picture from your Research Protection Program? Don't keep it to yourself! Why not share it with the DON Research Protection community? We're looking for material to publish in the *Research Protections Update* newsletter. Send your research news, success stories, tips, pictures, lessons learned, or other material related to the ethical conduct of human research to usn.ncr.bumedfchva.mbx.don-hrpp@mail.mil.

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